Remarks

The invention relates to devices for conducting assays, including qualitative, semi-quantitative and quantitative determinations of a plurality of analytes in a single test format. Claims 74-100 are currently pending in the application. Applicant has amended claims 74, 75, 89, 90, 95, and 96 herein. These amendments do not alter the scope of the claims, but rather are intended for the benefit of the Examiner in understanding the instantly claimed invention.

Notwithstanding the foregoing, Applicant expressly reserves the right to pursue subject matter no longer claimed in the instant application in one or more applications which may claim priority hereto. Applicant respectfully requests reconsideration of the claimed invention in view of the foregoing amendments and the following remarks.

Art-Based Remarks

35 U.S.C. § 102

Applicant respectfully traverses the rejection of claims 74-100 under 35 U.S.C. §102 (b), as allegedly being anticipated by Hillman et al., U.S. Patents 4,756,884 or 4,948,961 ("the Hillman patents").

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the teaching of the specification. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). *See also*, MPEP §2131. A patentee is free to be his or her own lexicographer and provide a particular meaning to a term or a phrase used in a claim, so long as that meaning is made clear in the specification or file history. *See*, MPEP § 2173.05(a).

The Examiner's rejection is based upon a flawed interpretation of the instantly claimed invention. In particular, the Examiner has responded to Applicant's previous remarks that the Hillman patents do not disclose a surface comprising a plurality of discrete capture zones corresponding to a plurality of different analytes, by arguing that "the claim language is only

directed to a plurality of target ligands and not a plurality of different target ligands." Paper No. 11, page 2. Thus, the Examiner appears to have taken the position that the phrase "a plurality of target ligands" does not refer to different ligands, and that this phrase might refer to a number of molecules of the same ligand. The Examiner does not provide any evidence that the skilled artisan would apply this meaning to the phrase "a plurality of target ligands." Instead, the Examiner merely asserts that it is so. Applicant respectfully submits that this is not a reasonable interpretation of the phrase.

The skilled artisan would understand that a "target ligand" is an analyte - one particular molecular species, which may exist as many molecules of the same species - that is the subject of detection in an assay. The skilled artisan would also readily acknowledge that a reference to assays measuring more than one target ligand do not refer to discrimination amongst individual identical molecules, but rather the detection of different molecular species. Thus, a "plurality of target ligands" as recited in the instant claims refers to two or more different molecular species that are detected in an assay, and not two or more molecules of a single ligand. Such assays are described, for example, in the instant specification on page 5, lines 30-32, which indicates that the devices described provide "the ability to detect at least one target ligand or a conjugate in an amount related to the presence or amount of target ligand in a sample."

Moreover, even if it is true that the phrase "plurality of target ligands" may, without more, be interpreted in the manner to which the Examiner refers, Applicant respectfully submits that a patentee is free to be his or her own lexicographer in providing a meaning to a phrase, so long as that meaning is made clear in the specification or file history. *See*, MPEP § 2173.05(a). In the previous response, Applicant distinguished the Hillman patents by stating that the instant claims refer to a plurality of discrete capture zones corresponding to a plurality of different analytes. Thus, Applicant has clearly indicated that, for purposes of the present application, the phrase "a plurality of target ligands" refers to different ligands. The Examiner's assertion to the contrary fails to properly consider the meaning of this term that has been made clear in the instant file

history. To the extent that the Examiner believes that Applicant has not yet made this meaning clear, Applicant now does so.

Applicant has also amended the pending claims herein to explicitly recite the phrase "a plurality of different target ligands." Applicant respectfully submits that this amendment is not made for purposes of patentability, but merely to assist the Examiner in understanding the meaning of a phrase that is already present in the instant claims from the existing language.

When the instant claims are properly interpreted, it is clear that the Hillman patents do not disclose a single non-absorbent surface within a capillary space comprising a plurality of discrete (*i.e.*, discontinuous) capture zones corresponding to a plurality of different analytes. The Examiner contends that columns 20 and 21 of the Hillman patents "use a variety of reagents for the detection of a variety of different analytes." Whether or not this is true, however, is irrelevant to the instant claims. The Examiner has failed to address each and every element of the instant claims, which refer to a diagnostic element comprising a capillary space; a non-absorbent surface in that capillary space; and a plurality of discrete capture zones on that non-absorbent surface corresponding to the plurality of target ligands. Thus, no *prima facie* case of anticipation has been established. *See*, MPEP § 2131 (in order to anticipate a claim, the identical invention must be shown in as complete detail as is contained in the claim).

As described by Applicant in the prior response, Applicant respectfully submits that, in those embodiments in which the Hillman patents disclose detection of more than one analyte, the Hillman patents disclose separating the flow into multiple capillary spaces, none of which detects more than a single analyte. *See, e.g.*, description of figure 4 in the '961 patent, column 21, lines 37-68 ("Chamber 28 is divided into two half chambers... 136 and 138."). Thus, the Hillman patents do not disclose any assay devices comprising a plurality of discrete capture zones on a single non-absorbent surface in a capillary space for determining the presence or amount of a plurality of target ligands in a sample, as provided by the instant claims.

Furthermore, the present claims refer to "a non-absorbent surface comprising a plurality of discrete capture zones." Nothing in the Hillman patents indicates that any one surface, bead or otherwise, contains a plurality of discrete (*i.e.*, discontinuous) capture zones for different analytes. In particular, the "beads" disclosed by the Hillman patents do not comprise discrete capture zones on their own surfaces; nor are they immobilized on a single nonabsorbent surface to provide discrete capture zones. *See, e.g.*, description of figure 3 in the '961 patent, column 20, line 47, through column 21, line 24 (For the detection of multiple analytes, beads in chamber 108 bind to a common epitope. In each of three separate chambers 96, 98, and 100, beads corresponding to individual serotype antigens are used to agglutinate the beads originating in (and flowing from) chamber 108 if that serotype is present in the original sample. Detection of another (undisclosed) anaylte in the sample may take place in yet another chamber 106).

Thus, the Hillman patents make it clear that any detection of multiple analytes must occur in separate spaces, and not in a common capillary space comprising a plurality of discrete capture zones on a surface. Because the Hillman patents do not teach and suggest every limitation of the claimed invention, the claims in the instant application are not anticipated by the cited patents. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully submits that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the telephone number listed below so that they may be resolved without the need for an additional action.

Respectfully submitted,
FOLEY & LARDNER

Dated: September 24, 2002

By: _____
For Richard J. Warburg,
Michael A. Whittaker
Registration No. 46,230

P.O. Box 80278
San Diego, CA 92138
Telephone: (858) 847-6721

Appendix A: Marked-up version of claims, showing amendments

74. (Amended) An assay device for determining the presence or amount of a plurality of different target ligands in a sample, the device comprising:

a diagnostic element comprising a capillary space through which said sample flows, comprising (i) a non-absorbent surface within said capillary space, and (ii) a plurality of discrete capture zones on said nonabsorbent surface, each discrete capture zone comprising a capture element that binds one target ligand in said plurality of different target ligands.

75. (Amended) The assay device of claim 74, comprising at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

76. (Reiterated) The assay device of claim 74, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

77. (Reiterated) The assay device of claim 74, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

78. (Reiterated) The assay device of claim 74, wherein said device further comprises a chamber fluidly connected to said diagnostic element, and a time gate that delays fluid flow between said chamber and said diagnostic element.

79. (Reiterated) The assay device of claim 74, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

80. (Reiterated) The device of claim 79 wherein the particles are latex.

81. (Reiterated) The device of claim 79 wherein the particles are polystyrene.

82. (Reiterated) The device of claim 79 wherein the particles are nanoparticles.

83. (Reiterated) The device of claim 82 wherein the nanoparticles comprise silica, zirconia, alumina, titania, ceria, metal sols, or polystyrene.

84. (Reiterated) The device of claim 82 wherein the nanoparticles have sizes in a range from about 1 nm to 100 nm.

85. (Reiterated) The device of claim 82 wherein the nanoparticles are immobilized on said nonabsorbent surface through adsorption or covalent bonds.

86. (Reiterated) The device of claim 79 wherein said particles are immobilized on said nonabsorbent surface by magnetic means, hydrophobic means, hydrogen bonding, electrostatic means, or entrapment.

87. (Reiterated) The device of claim 79, wherein said particles have diameters ranging from about 0.1 mm to 10 mm.

88. (Reiterated) The device of claim 79, wherein said receptor is immobilized on a surface of the particle.

89. (Amended) A method for determining the presence or amount of a plurality of <u>different</u> target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a labeled reagent that binds to said plurality of target ligands,

whereby said sample and said labeled reagent flow through said capillary space for capture of each said <u>different</u> target ligand at its corresponding capture zone; and

generating a plurality of detectable signals from label bound to each different target ligand at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of different target ligands in said sample.

90. (Amended) The method of claim 89, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

91. (Reiterated) The method of claim 89, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

92. (Reiterated) The method of claim 89, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

93. (Reiterated) The method of claim 89, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

94. (Reiterated) The method of claim 89, wherein said labeled reagent is a fluorescently labeled reagent.

95. (Amended) A method for determining the presence or amount of a plurality of different target ligands in a sample, the method comprising:

contacting the diagnostic element of claim 1 with

(i) a sample, and

(ii) a plurality of ligand analogue conjugates, each ligand analogue conjugate corresponding to one of said plurality of different target ligands,

whereby said sample and said plurality of ligand analogue conjugates flow through said capillary space, whereby each different target ligand competes with its corresponding ligand analogue conjugate for capture at its corresponding capture zone; and

generating a plurality of detectable signals from ligand analogue conjugate bound at its corresponding capture zone, whereby said signals are related to the presence or amount of said plurality of different target ligands in said sample.

96. (Amended) The method of claim 95, wherein said diagnostic element comprises at least 50 said discrete capture zones, corresponding to at least 50 different target ligands.

97. (Reiterated) The method of claim 95, wherein said nonabsorbent surface comprises a width dimension substantially perpendicular to the direction of fluid flow through the capillary space, and wherein each said discrete capture zone spans said width dimension.

98. (Reiterated) The method of claim 95, wherein said capture element is selected from the group consisting of an antibody or binding fragment thereof, a nucleotide sequence, an enzyme, a chelator, and a biosensor.

99. (Reiterated) The method of claim 95, wherein said discrete capture zones comprise particles immobilized thereon, wherein said particles comprise said capture element immobilized thereon.

100. (Reiterated) The method of claim 95, wherein said ligand analogue conjugate is a fluorescently labeled ligand analogue conjugate.